Profile

Mary Lyon: quiet battler

Gail Vines

Mary Lyon discovered X-inactivation — the process that enables female mammals to avoid genetic overdose by randomly switching off one X chromosome in each of their cells — some 40 years ago. In the past 20 years, she has received six awards in recognition of this discovery, including the recently announced Wolf Prize in medicine, worth US$ 100,000. At 71, Lyon will use the award to continue her work at the Medical Research Council's Mammalian Genetics Unit at Harwell, south of Oxford in England.

Her colleagues say she is quiet, unassuming, yet utterly determined. For years she ruled the genetics division at Harwell with a "very firm hand". Her conversation is often punctuated by "great long periods of silence," but there is no need to panic; she is thinking. "Mary is really an exceptional scientist — incredibly disciplined and able to see right through a problem," says Bruce Cattanach, director of the Mammalian Genetics Unit, formerly known as the Radiobiology Unit.

The problem puzzling Lyon 40 years ago centred round a ragbag of 'mosaic' anomalies that cropped up only in female mammals. The radiation experiments that were her 'bread-and-butter' had produced strains of mice in which only the females had oddly spotted fur. Lyon paid attention to these mice, not least because she "really likes mice," says Cattanach. "She goes in to talk to them, she is very sweet with the animals." With the help of the mice, she published the solution to the puzzle in *Nature* on 22 April 1961. At the time, J.B.S. Haldane said: "I wish I had thought of it."

Scientists in North America were quick to appreciate the beauty of Lyon's idea and to see its relevance to sex-linked genetic diseases in humans. "Geneticists hail new hypothesis," trumpeted the *New York Times*, when Lyon visited Manhattan in 1963 to attend a conference on congenital malformations. The "unexpected heroine" of the meeting, said *Time* magazine, was "a quiet Englishwoman who presented no paper and who is, of all things, editor of the semi-annual *Mouse News Letter*". For years, X-inactivation was called 'Lyonization', though Lyon herself disapproved of the tag.

Back at home, however, Lyon was slower to gain the plaudits she deserved. A leading mouse geneticist of the day, Professor Hans Grüneberg, launched a "savage" campaign to discredit her, but "Mary was tough — she kept coming back," says Cattanach, and eventually Grüneberg conceded defeat. Yet his influence may have delayed Lyon's election to the Royal Society — she was at last made a Fellow in 1973.

It was a "very difficult and very depressing" time for Lyon, who had first come into contact with Grüneberg in 1950 when he examined her PhD thesis. Eleven years on, "he may not have realised I wasn't a PhD student any more — that I didn't have to ask him for permission," speculates Lyon. Misogyny may also have played its part.

Peer review could have been her downfall, but in those days, *Nature* did not invariably send papers out to referees. "It is interesting to speculate whether I would ever have managed to get it published if they had," muses Lyon. Grüneberg would have been the obvious person to review the paper.

As it was, Lyon had had to fight her corner even to be allowed to do the research that led up to the discovery of X-inactivation. The MRC's Radiobiology Unit was set up in the aftermath of Hiroshima, to study the genetic effects of radiation. "We were under a lot of pressure to concentrate almost entirely on

Mary Lyon at her 'retirement' party at Harwell in 1990

standard radiation work," Lyon remembers. Yet she knew that the mutants thrown up by the irradiation experiments could also provide valuable insights into fundamental genetics, at a time when mouse genetics was poorly understood. "The MRC is so proud of this work now, but she battled for it," says Cattanach.

But fighting battles was nothing new to Lyon. At school during the war years, she struggled to be allowed to do science A-level examinations, only to gain a place at Cambridge University in the days when that august institution did not officially award degrees to women. Intrigued by C.H. Waddington's writings about genes and development, she embarked in 1946 on a challenging PhD in mouse genetics, about which almost nothing was known at the time. Early in her third year, however, the genetics professor, R.A. Fisher, "withdrew the facilities I was using — a primitive lab — to turn it over to bacterial genetics". She found shelter in Waddington's "stimulating and supportive" group in Edinburgh, and stayed on to begin work on the genetic effects of radiation, funded by the MRC. In 1955, she moved with the group when it was transferred to larger facilities at Harwell, where she found secure funding but more pressure to concentrate on radiation hazards.

If pressures for routine radiological research once threatened to displace innovative genetic investigations, today it is an overweening emphasis on molecular work that distorts the research agenda. “People who understand how to do classical genetics with mice are very thin on the ground,” says Lyon. Even worse, the future of mutant mouse lines throughout the world is far from secure. “Grant-givers tend not to want to pay money to keep genetic stocks going, even though so much is coming out of mouse genetics,” Lyon says. “But if only we can keep the battle going, the pendulum may swing back as people recognize the importance of keeping all this going.” Let us hope she wins this battle too.

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Turning points

The short step from physics to ecology

Robert M. May

The ‘paper’ which changed the whole direction of my life in scientific research was not a journal article but rather a chapter in Ken Watt’s book, *Ecology and Resource Management* [1].

I read it in 1970, shortly after being appointed to the University of Sydney’s first Personal Chair, in theoretical physics. I had, over the preceding few years in Sydney, been involved in founding the movement for Social Responsibility in Science (SRS) — this, remember, was the late 1960s — and reading Watt’s book was part of a programme of informing myself of what we were being socially responsible about.

Ken Watt’s chapter, *The principles of ecology*, set out very clearly the conventional wisdom of the time, that “complex ecosystems are more stable”. Watt first summarized Charles Elton’s influential arguments to this effect, but then confessed to scepticism, citing, *inter alia*, examples of insect populations which fluctuated dramatically despite complex multispecies interactions.

As I read this, at home one evening, I was drawn to one of Elton’s observations in particular: simple models of one-prey–one-predator associations (Lotka–Volterra or Nicholson–Bailey models in the jargon of the trade) either show population oscillations or gross instability. But this is not an argument, I thought. The question is: do the corresponding n-prey–n-predator models tend to be less subject to fluctuation as n increases? A brief calculation showed the contrary. As a mathematical generality, the more species in a simple Lotka–Volterra prey–predator system, the less likely it is to persist.

The next day, I shared this overturning of one of Elton’s arguments with a colleague at the University of Sydney. This was no ordinary colleague; Charles Birch, Challis Professor of Biology and founding president of SRS, was co-author of one of the most influential ecology books of the third quarter of the century. He also knew Ken Watt well.

Birch’s personal belief was that mathematical approaches had little to contribute to ecology, but his generosity of spirit was such that, unlike many people, he never discouraged colleagues because he disagreed with them. He encouraged me to write to Ken Watt, who in turn encouraged a short paper on my evening’s work for *Mathematical Biosciences*.

Soon after, I spent a sabbatical year at Culham, the plasma physics laboratory near Oxford in England, and in the USA at the Institute for Advanced Studies, Princeton University. Although I was still mainly occupied with theoretical physics, Charles Birch had put me in touch with ecologist friends in the UK (Richard Southwood, John Maynard Smith and George Varley) and at Princeton (Robert MacArthur), and, as a result, I came across many interesting new problems. Over the next couple of years, this led to work on a variety of questions concerning the dynamical behaviour of populations and communities of plants and animals [2]. Some of this work helped chaos to move centre stage as a new discipline. In 1973, I moved to Princeton as Professor of Biology, following Robert MacArthur’s untimely death.

To me, this entire story is a striking instance of, as it were, ‘sensitivity to initial conditions’ in our own lives. The great fun and good fortune I have enjoyed as a theoretical ecologist over the past 25 years derive mainly from the lucky accident of being in the right place at the right time; of stumbling into a subject as key questions were being phrased analytically, but by people who largely lacked the mathematical skills to pursue the analysis. Equally, the many influential people — Watt, Birch, Southwood, MacArthur, and many others — who generously welcomed a new player and new ideas, helped to make the step from physics to ecology an easy one.

References

1. Watt K: *Ecology and Resource Management.* New York: McGraw-Hill; 1968.
2. May RM: *Stability and Complexity in Model Ecosystems*. Princeton: Princeton University Press; 1973.

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The editors of *Current Biology* have invited a number of biologists to reveal the papers that have influenced them most profoundly in their careers. These brief essays will be published in future issues. If you have any comments, or ideas arising from this series, we shall be happy to consider them.